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## NR DELAYS VINCRISTINE-INDUCED AXON DEGENERATION IN DORSAL ROOT GANGLIA CULTURES

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Chemotherapy-induced peripheral neuropathy (CIPN) is a common and dose-limiting side effect of anti-cancer therapies. CIPN symptoms include numbness in hands and feet, shooting and burning pain in arms and legs, and muscle weakness, which can extend beyond the time of treatment and may cause permanent disability. Many CIPNs are primarily characterized by axon dysfunction and/or degeneration. Recent work from the laboratories of Jeffrey Milbrandt and Aaron DiAntonio has shown the protective effect of the genetic deletion of SARM1 (sterile alpha and TIF motif containing protein 1) on acute axon degeneration (AxD). In axotomy experiments, SARM1 is regulated by the activation of a MAP kinase cascade and acts through the decrease of NAD<sup>+</sup>. However, CIPN causes subacute/chronic axonal loss, so it may work through a different pathway than acute injury by axotomy. To gain insight into mechanisms of axonal loss in CIPN, we use the chemotherapy drug vincristine to induce AxD in murine dorsal root ganglia cultures. We evaluated the effectiveness of drugs that disrupt the SARM1 pathway in axotomy to examine if vincristine acts through a similar SARM1-mediated AxD pathway following vincristine. We show that there is a significant decrease of vincristine-induced AxD with the treatment of NR, and there is additional protection with a combination of NR and JNKi, consistent with previous research on the protective effect of MAPK inhibitors and NAD<sup>+</sup> precursors in delaying acute AxD. This suggests that drugs that disrupt the SARM1 pathway can be therapeutic in delaying chronic axonal injury induced by vincristine, and potentially other CIPNs.